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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,354	06/30/2004	Masayo Higashiyama	2004_1016A	2612

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EXAMINER	
FRAZIER, BARBARA S	
ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
11/30/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/500,354	HIGASHIYAMA, MASAYO	
	Examiner	Art Unit	
	BARBARA FRAZIER	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-10,12 and 13* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-10,12 and 13* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-10, 12, and 13 are pending in this application. Claim 11 stands canceled.

2. Claims 1-10, 12, and 13 are examined.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-10, 12, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kita et al (US Patent 6,307,052, previously cited) in view of Lehmussaari et al (US Patent 5,795,913).

The claimed invention, as amended, is drawn to an aqueous liquid preparation comprising, in an aqueous solution, an active ingredient consisting of (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid (i.e., bepotastine) or a pharmaceutically acceptable acid addition salt thereof, and a water-soluble metal chloride in a light stabilizing effective amount of 0.2 w/v% or more (see claim 1).

Kita et al teach that the benzenesulfonic acid salt or benzoic acid salt of (S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butanoic acid (i.e., bepotastine) is

excellent in antihistaminic activity and antiallergic activity, has little hygroscopicity and excellent in physicochemical stability, so that it is particularly suitable compound as a medicine. Kita et al also teach that its present invention relates to a medical composition containing the compound as an effective ingredient (see col. 1, lines 10-22).

While Kita et al teach a medical composition comprising bepotastine, Kita et al do not specifically teach how the composition is formulated, and do not specifically teach a water-soluble metal chloride in a light stabilizing effective amount of 0.2 w/v% or more.

Lehmussaari et al teach an ophthalmic composition in the form of a topical aqueous solution consisting essentially of an ophthalmologically active agent containing basic groups, an ion sensitive hydrophilic polymer containing acidic groups, and at least one salt selected from the group of inorganic salts and buffers in a total amount of from 0.01 to 2.0% by weight (abstract). The ophthalmologically active agent may be an antiallergic agent containing basic groups, including basic heterocycles, such as pyridine and piperidine (col. 4, lines 2-9). The salt/buffer functions as a viscosity reducing agent; choices of salts include sodium chloride and potassium chloride (col. 3, lines 45-50 and claim 5). The composition is administered as a liquid and obtains a desired beneficial effect of the active agent in the eye, while simultaneously reducing any discomfort in the patient's eye, as compared to the administration of a composition in gel form. The composition also provides for an additional wetting effect while providing for a better contact and thus a controlled absorption of active agent into the eye (col. 2, lines 10-18).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to formulate the medical composition of Kita et al with the aqueous solution of Lehmussaari et al; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because the aqueous solution of Lehmussaari et al provides the benefits of better contact and controlled absorption of active agent into the eye, as well as additional wetting effect, as taught by Lehmussaari et al (col. 2, lines 10-18). One would reasonably expect success from the use of the formulation of Lehmussaari et al to formulate the medical composition of Kita et al because Lehmussaari et al teaches that the opthalmalogically active agent may be an antiallergic agent containing basic groups such as pyridine and piperidine, and Kita et al teach that its compounds have excellent antiallergic activity, and contain both pyridine and a piperidine groups.

Regarding the limitations, "a water-soluble metal chloride in a light-stabilizing effective amount of 0.2 w/v% or more" (claim 1), "sodium chloride at not less than 0.2 w/v% and not more than 0.8 w/v% in a light-stabilizing effective amount" (claim 10), and "light-stabilized with a water-soluble metal chloride at not less than 0.2 w/v% (claim 13), as well as other particular amounts claimed (claims 2, 4, and 13), Lehmussaari teaches an amount of buffer/salt from 0.01 to 2.0% by weight (col. 2, lines 65-67) which functions to reduce the viscosity, which is favorable for both efficacy and ease of application (col. 3, lines 35-40). This range overlaps those of the claimed invention; one skilled in the art would be motivated to manipulate the amount of salt from within said ranges, including the ranges claimed, by routine experimentation, in order to optimize

the viscosity reducing effect of the salt. Such amounts would necessarily be a light-stabilizing effective amount, as evidenced by Applicant's specification (e.g., see page 2, line 27 – page 3, line 10).

Regarding the choice of metal chloride (claims 3, 10, and 12) Lehmussaari et al teach six choices of buffer/salt, two of which are sodium chloride and potassium chloride (col. 3, lines 45-50), and exemplify sodium chloride as the salt present in the composition (col. 5, Example 2).

Regarding claims 5 and 6, Kita et al teach the benzenesulfonic acid salt of bepotastine (col. 1, lines 11-13).

Regarding claim 7, Lehmussaari et al teach that the pH of the composition is suitably from 5 to 8 (col. 3, lines 59-60), which is within Applicant's range.

Regarding the limitation that the composition is an eye drop (claims 8, 10 and 13), Lehmussaari et al teach that its invention is an easy-to-use eye drop formulation with improved patient compliance (col. 2, lines 3-5).

Regarding the limitation that the composition is a nasal drop (claim 9), said limitation recites an intended use of the composition. Since the components of the composition of the combined references are suitable for use in the nose, said composition would be capable of use as a nasal drop.

Response to Arguments

5. Applicant's arguments filed 6/10/11 have been fully considered but they are not persuasive.

Applicant argues the ion sensitive, hydrophilic polymer of Lehmussaari, such as Carbopol, would materially affect the basic and novel characteristics of the aqueous liquid preparation of the claimed invention, citing WO 2009/142950 ("WO '950"), which teaches a higher NTU value for an aqueous solution of Carbomer (i.e., Carbopol) and sodium chloride, as compared to the same solution which does not include sodium chloride.

This argument is not persuasive. It is first noted that Applicant's specification teaches that other same or different kinds of efficacious ingredients may be added appropriately as long as the object of the present invention is not impaired (page 6, lines 22-25 of the specification). It is also noted that the WO '950 patent has a publication date of 26 November 2009 and a filing date of 12 May 2009, both of which are well past the filing date of the instant application (30 June 2004). Applicant has not indicated any teaching in the specification which teaches the polymer of Lehmussaari would materially affect the basic and novel characteristics of the claimed invention, or would impair the object of the present invention, or that the basic and novel characteristics of the claimed invention exclude ion sensitive hydrophilic polymers from the "efficacious ingredients" which may be included in the composition. Lehmussaari teaches hydrophilic polymers, such as Carbopol, are useful with ophthalmologically active agents and salts in ophthalmic compositions. Therefore, *at the time the invention was made*, it still would have been obvious for a person having ordinary skill in the art to formulate the medical composition of Kita et al with the aqueous solution of Lehmussaari et al; thus arriving at the claimed invention.

Even if the teachings of the WO '950 patent were applicable, it is noted that the WO '950 patent only teaches a higher NTU when the aqueous solution comprises only carbopol and sodium chloride; however, when other ingredients are added, such as povidone, the NTU value decreases. Lehmussaari teaches solutions of Carbopol and sodium chloride are, in fact, suitable as ophthalmic compositions (e.g., see Example 2), and therefore one skilled in the art would reasonably expect success from formulating formulate the medical composition of Kita et al with the aqueous solution of Lehmussaari et al.

In response to Applicant's arguments that Lehmussaari teaches that "for appearance and storage purposes, the use of a buffering salt is preferred to the use of e.g. sodium or potassium chloride as the viscosity reducing agent", it is noted that Lehmussaari specifically names only six viscosity reducing agents, the first two named being metal chlorides (col. 3, lines 45-50), and therefore one skilled in the art would clearly envisage the use of a metal chloride. Even if a buffering salt may be preferred, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

In response to Applicant's arguments that the references do not teach or suggest the light-stability or the light-stabilization of a drug, it is noted that the amounts of buffer/salt of Lehmussaari (used to control viscosity) overlap those of the claimed invention, such that one skilled in the art would be motivated to manipulate the amount of salt from within said ranges, including the ranges claimed, by routine

experimentation, in order to optimize the viscosity reducing effect of the salt. Such amounts would necessarily be a light-stabilizing effective amount, as evidenced by Applicant's specification (e.g., see page 2, line 27 – page 3, line 10). Applicant has not pointed to any evidence demonstrating the criticality of the claimed range of amounts for providing a light-stabilizing effect, or that amounts falling within the amounts of Lehmussaari but outside those of the claimed invention do not provide a light-stabilizing effect.

Therefore, it is the position of the Examiner that the claims are rendered obvious.

Conclusion

No claims are allowed at this time.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Friday 9am-2:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/Joanne Hama/
Primary Examiner, Art Unit 1632